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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/928,757	09/12/1997	GEERT MAERTENS	1487-17	1001

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EXAMINER	
CLOW, LORI A	
ART UNIT	PAPER NUMBER
1631	

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19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/928,757	Applicant(s) MAERTENS ET AL.
	Examiner Lori A. Clow, Ph.D.	Art Unit 1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *65-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *65-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' arguments, filed 15 May 2001, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims Rejections-35 USC 112

Claim 66 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to make and/or use elected SEQ ID Nos. 53, 56-59, 66-68, 72, 73, 82, 83, and 86-88, presumably for the treatment of HCV. However there are no particulars disclosed as to how to practice this. The only mention of these sequences is on page 21-22, 32-33 and associated tables in the

specification, as filed. For the reasons discussed below, there would be an unpredictable amount if experimentation required to practice the claimed invention.

b) The specification provides examples for generic methods for using the disclosed sequences in a variety of different molecular assays.

c) The specification provides no working examples of using said sequences in any particular manner, especially not for the treatment of HCV. There is no evidence that these sequence is connected to the amelioration of HCV or it's symptoms.

d) The invention is drawn to SEQ ID Nos. 53, 56-59, 66-68, 72, 73, 82, 83, and 86-88.

e) It would have been well known in the art at the time the invention was made that these peptides, supposedly to be used for therapeutic intervention in HCV, would have to show protective immunity of some sort. This could be done by viral load experimentation in a model system. The specification, however, provides no indication of protection, treatment, abolishment of HCV with said peptides. The state of the art for HCV suggests that protective therapies are not obtainable. For example, Farci et al. (Science (1992) vol.258:135-140) analyzes viremia and humoral immune response in chimpanzees inoculated with different HCV strains derived from different individuals. After viral challenge all animals developed classical hepatitis. The second-generation test revealed that none of the animals developed antibodies to E2. The conclusion is that the virus or components thereof fails to induce protective immunity against reinfection with HCV, possibly due to lack of neutralizing antibody response or due to the genetic variability that leads to the rapid development of escape mutants that are able to circumvent the immune response. Given the lack of success in the art, and the lack of working examples, the specification is not enabling.

f) The skill of those in the art of virology is high.

g) The prior art indicates lack of success in the area of therapeutic compositions for HCV.

h) The claims are broad because they are drawn to a variety of peptides and not to any particular peptide with a particular purpose.

The skilled practitioner would first turn to the instant specification for guidance to use said sequences. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art shows that therapeutic compositions for HCV are not obtainable. Finally, said practitioner would turn to trial and error experimentation. Therefore, while the skill of art in virology is high, the lack of information in the specification would lead one to undue experimentation of one of ordinary skill in the art to determine what, if any, use of said peptides was therapeutic.

Claims 65-76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the recitation "and **optionally** a pharmaceutically acceptable carrier" (all pending claims) it is unclear as to what is meant by optionally. Does it not matter if the carrier is there in order to practice said invention? How will the composition be effective as a therapeutic to treat mammals if there is no carrier?

In claims 69-72, what is meant by therapeutic? What exactly is being treated or alleviated or exacerbated?

In claims 75-76, it is unclear as to what is being treated in this method? Is HCV itself being treated or is a symptom of HCV being treated?

Claims Rejecions-35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 65 and 67-73 are rejected under 35 U.S.C. 102(a) as being anticipated by Choo et al. (PNAS (1994) vol. 91:1294-1298). Choo et al. disclose approximately 1.5 mg of purified E1/E2 glycoproteins that were obtained from 150 liters of infected HeLa cells. The purity was

greater than or equal to 80% (see Methods section, page 1294), encompassing the limitations of said claims.

Claim 66 is rejected under 35 U.S.C. 102(a) as being anticipated by WO 9318054-A, which discloses amino acids at positions 397-418 of SEQ ID NO. 72 of the instant application

Claim 66 is rejected under 35 U.S.C. 102(b) as being anticipated by the following US and WO documents: US 5,747,239, US 6,183,949, WO 9306247-A, and WO 9364205-A, as applied to the following SEQ ID Nos. of the instant application.

SEQ ID NO. 58 is anticipated by 5,747,239, which discloses SEQ ID Nos. 79 and 80, which contain the region consisting of amino acids 205 to 224, as required by claim 66.

SEQ ID NO. 66 is anticipated by US 5,747,329, which discloses SEQ ID Nos. 82 and 119, which contain the region consisting of amino acids 301 to 320, as required by claim 66.

SEQ ID NO. 66 is also anticipated by US 6,183,949, which discloses SEQ ID NO. 23, which contains the region consisting of amino acids 301-320, as required by claim 66.

SEQ ID NO. 66 is also anticipated by US 5,582,968, which discloses SEQ ID NO. 2, consisting of amino acid region 301-320, as required by claim 66.

SEQ ID NO. 82 is anticipated by US 5,747,239, which discloses SEQ ID NO. 43, which contains the region consisting of amino acids 523-542, as required by claim 66.

SEQ ID NO. 83 is anticipated by US 5,747,239, which discloses SEQ ID NOs. 2, 41, 42, and 43, all of which contain amino acids 547-566, as required by claim 66.

SEQ ID NO. 86 is anticipated by US 5,747,239, which discloses SEQ ID NO. 44, containing amino acids 583-602, as required by claim 66.

SEQ ID NO. 87 is anticipated by US 5,747,239, which discloses SEQ ID NO. 44, containing amino acids 595-614, as required by claim 66.

SEQ ID NO. 88 is anticipated by US 5,747,239, which discloses SEQ ID NO. 44, containing amino acids 607-626, as required by claim 66.

SEQ ID NO. 88 is also anticipated by US 5,308,750, which discloses SEQ ID NO. 2, containing amino acids 607-626, as required by claim 66.

SEQ ID NO. 88 is also anticipated by WO 9364204-A and WO 930627-A, disclosing the same as above.

Claims 65 and 67-73 are rejected under 35 U.S.C. 102(e) as being anticipated by Ralston et al. (US 6,274,148 B1). Ralston et al. disclose a recombinant glycoprotein selected from the group consisting of HCV E1 and E2 in combination with a pharmaceutically acceptable carrier (column 2, lines 53-58). This purifies protein(s) are at least about 80% of the total protein content (column 4, line1), as in claim 65, and 67-73.

Double Patenting-Obvious-type

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 65-74 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5, 8-17, and 21 of U.S. Patent No. 6,150,134. Although the conflicting claims are not identical, they are not patentably distinct from each other because the disclosed proteins of the instant application are the same as the disclosed E1, E2, E1/E2 proteins in US 6,150,134. They include a recombinant single or specifically oligomerized envelope viral protein selected from the group consisting of E1, E2, or E1/E2 viral proteins obtained by the methods steps outlined in the patent, as well as the instant application.

Applicant's arguments regarding the 35 USC 102 rejections have been considered. The rejections over Deleys (WO 93/18054, Houghton (EP 388232) and Miyamura (EP 537626) are withdrawn.

The rejection over Ralston (US 6,074,848) is withdrawn.

The rejection over Brechot (US 5,866,139) is withdrawn.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located

in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Bill Phillips, whose telephone number is (703) 305-3419, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

August 26, 2002

Lori A. Clow, Ph.D.
Art Unit 1631

Lori A. Clow

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